



**University of
Zurich**^{UZH}

**Zurich Open Repository and
Archive**

University of Zurich
University Library
Strickhofstrasse 39
CH-8057 Zurich
www.zora.uzh.ch

Year: 2013

Current outcome of acute coronary syndromes: data from the Zurich-Acute Coronary Syndrome (Z-ACS) Registry

Ghadri, J R ; Jaguszewski, M ; Sacron, A ; Srikantharupan, S ; Pfister, P ; Siddique, A ; Kaufmann, P
A ; Wyss, C A ; Gämperli, O ; Landmesser, U ; Altwegg, L ; Maier, W ; Corti, R ; Lüscher, T F ;
Templin, C

Posted at the Zurich Open Repository and Archive, University of Zurich

ZORA URL: <https://doi.org/10.5167/uzh-91028>

Journal Article

Published Version

Originally published at:

Ghadri, J R; Jaguszewski, M; Sacron, A; Srikantharupan, S; Pfister, P; Siddique, A; Kaufmann, P A;
Wyss, C A; Gämperli, O; Landmesser, U; Altwegg, L; Maier, W; Corti, R; Lüscher, T F; Templin, C
(2013). Current outcome of acute coronary syndromes: data from the Zurich-Acute Coronary Syndrome
(Z-ACS) Registry. *Cardiovascular Medicine*, 13(4):115-122.

Current outcome of acute coronary syndromes: data from the Zurich-Acute Coronary Syndrome (Z-ACS) Registry

Jelena R. Ghadri^{a,1}, Milosz Jaguszewski^{a,1}, Annahita Sacron^b, Shajanth Srikantharupan^a, Pascal Pfister^a, Asim Siddique^a, Philipp A. Kaufmann^a, Christophe A. Wyss^a, Oliver Gaemperli, Ulf, Landmesser^a, Lukas Altwegg^a, Willibald Maier^a, Roberto Corti^a, Thomas F. Lüscher^a, Christian Templin^a

^a Department of Cardiology, Cardiovascular Center, University Hospital Zurich, Switzerland

^b University of California Davis Medical Center, California, USA

Summary

Background: Acute coronary syndrome (ACS) encompasses ST-segment elevation myocardial infarction (STEMI), non-ST-segment myocardial infarction (NSTEMI) and unstable angina (UA). Although initially a syndrome with a poor prognosis, the advent of acute percutaneous coronary intervention (PCI), with novel stents and anticoagulation therapy, as well as the establishment of acute chest pain units, has to a great extent improved the outcome for patients with ACS.

Objective: The aim of the present study was to assess the 30-day outcome for patients with ACS admitted to the University Hospital of Zurich, and to compare the data, particularly for in-hospital death, with results from various other registries, such as the international Global Registry of Acute Coronary Events (GRACE).

Methods: Between 2007 and 2010, we included consecutive patients with a diagnosis of ACS, examined in-hospital death and major adverse cardiac events (MACE) at 30-days, and compared our results with the esteemed GRACE-Registry.

Results: During these 4 years, 1,787 consecutive patients were diagnosed with ACS. Of these, 55.8% (n = 998) had STEMI, 35.3% (n = 631) NSTEMI and 8.8% (n = 158) UA. In contrast, in the GRACE, out of 11 543 patients 30% (n = 3419) had STEMI, 25% (n = 2893) NSTEMI and 38% (n = 4397) UA. The in-hospital death rate in our study group was 5.7% with STEMI, 2.5% with NSTEMI and 1.3% with UA (p = 0.001). Hospital case fatality rates for STEMI, NSTEMI and UA from the GRACE were 7%, 5% and 3%, respectively

(p < 0.01). At the University Hospital of Zurich, myocardial infarction occurred in 1.6%, 0.5% and 1.3% of the STEMI, NSTEMI and UA groups, respectively (p = 0.120), compared with 3% with STEMI and 2% with NSTEMI in the GRACE (data for UA not available). Cardiogenic shock was present in 8.7%, 5.4% and 0.6% (p < 0.001) at the University Hospital of Zurich compared with 7%, 5%, and 2% (p < 0.01) in patients from the GRACE for STEMI, NSTEMI and UA, respectively. Kaplan-Meier survival analysis including MACE revealed that patients with STEMI had the most unfavourable outcome when compared with NSTEMI and UA (p = 0.018).

Conclusions: Our results indicate that patients with ACS from the “real-world” Zurich registry show a higher rate of STEMI and yet lower event rates for adverse cardiovascular complications and in-hospital death when compared with the GRACE, which may be explained by the high standard of healthcare at this institution and implementation of novel therapeutic strategies.

Key words: acute coronary syndrome; outcome; registry

Introduction

Acute coronary syndrome (ACS) constitutes a spectrum of clinical presentations such as ST-segment elevation myocardial infarction (STEMI), non-ST-segment myocardial infarction (NSTEMI) and unstable angina (UA) [1]. ACS is most commonly caused by rupture of a vulnerable atherosclerotic plaques [2], al-

Funding / potential competing interests: The study was supported in part by a grant of the Swiss National Science Foundation (SNSF) «Sonderprogramm Universitäre Medizin» [Nr. 33CM30-124112/1]. The institution of the authors has received grants from AstraZeneca, Switzerland, Biosensors, Switzerland, Eli Lilly, Indianapolis, USA, Medtronic and St. Jude, Switzerland.

¹ **Authors' contribution:** JRG and MJ contributed equally to this work.

Correspondence:
Christian Templin, MD, PhD
Attending Physician
Department of Cardiology
University Hospital of Zurich,
Raemistrasse 100
CH-8091 Zürich
Christian.Templin[at]usz.ch

though ulceration, fissuring, erosion or dissection with intraluminal thrombus formation may also be involved. All these presentations are referred to as myocardial infarction (MI) type 1 according to the European Society of Cardiology classification by Thygesen et al. [3]. Advances in medical therapy, and large clinical trials and the guidelines established in consequence, have substantially improved the treatment of ACS over recent past decades. Nonetheless, ACS remains the leading cause of morbidity and mortality worldwide and such cardiovascular disease accounts for 17.3 million deaths per year [4].

Attempts have been made to evaluate hospital management and clinical outcomes using registries in order to monitor and improve the quality of care [5]. It is noteworthy that, in spite of available guidelines [6] on the management of ACS, current practice differs between hospitals and countries; as a consequence, differences in outcomes for patients with ACS between centres and countries have been noted [7]. Furthermore, although randomised clinical trials are the gold standard of evidence-based medicine, the patient population in clinical trials may not truly represent “real life” patients [8]. Indeed, Steg et al. found that ineligible patients in randomised controlled trials had the highest mortality, while eligible participants showed the lowest mortality [9]. Similarly, Bosch and colleagues reported that patients who were excluded from a randomised trial assessing the outcome of NSTEMI had a worse risk profile, more comorbidities and a nearly three-fold higher mortality rate compared with eligible patients [10]. Consequently, registries are of significant importance in outcome evaluation of ACS. The Global Registry of Acute Coronary Events (GRACE) is a prospective, multinational study of patients with ACS which was launched in 1999, and which currently includes 30 participating countries and over 100,000 patients [11, 12]. However, even in such registries, the real world may not be fully reflected, as patients with shock are often not included.

Here, we present the acute and short-term outcome for all consecutive patients with ACS enrolled in the Zurich-Acute Coronary Syndrome Registry (Z-ACS), within a 4-year period. Thus, this patient cohort truly represents the real-world population seen in an urban tertiary centre, including sudden-death survivors and patients in cardiogenic shock. Furthermore, we compared in-hospital death and major adverse cardiovascular events (MACE) at 30 days, as outcome measures of this single-centre registry with those of the international GRACE registry.

Methods

Data collection

From 2007 to 2010, we included consecutive patients who were admitted with a diagnosis of ACS to the Uni-

versity Hospital of Zurich and who underwent coronary angiography. As at this institution thrombolysis has been abandoned and all ACS patients are referred for angiography, this represents the true ACS population. All patients enrolled in this registry were at least 18 years of age. The time period of the inclusion of patients in our registry covered three redefinitions of myocardial infarction [13, 14]. However, because of the retrospective nature of the study we used the current definition of myocardial infarction of 2012 [15]. Retrospectively, data were collected using KISIM® (Klinik Informations System Innere Medizin), an in-hospital software system. The data included baseline characteristics such as cardiovascular risk factors, patients' cardiovascular medication on admission and laboratory values. Coronary artery disease (CAD) was classified as single vessel or multivessel disease, and the culprit lesion was documented and categorised in the following manner: left main artery, left ascending artery, circumflex artery, right coronary artery or bypass graft disease. Furthermore we recorded haemodynamic parameters such as blood pressure, heart rate, left ventricular enddiastolic pressure and left ventricular ejection fraction. Data were retrospectively analysed as part of the quality control at the University Hospital of Zurich.

Short-term follow-up

The occurrence of MACE, including in-hospital death, revascularization, coronary artery bypass graft (CABG), nonfatal myocardial infarction, stent thrombosis, cardiogenic shock, stroke and septic shock, was assessed at the 30-day follow-up. ACS was defined as typical angina, elevated cardiac enzymes and/or typical ECG changes. Stroke was recorded after the case was reviewed independently by a neurologist and was defined as focal neurologic deficits lasting longer than 24 hours with a clinically relevant lesion on brain imaging. The second endpoint included in-hospital death.

Statistical analysis

Baseline characteristics and outcomes for the three patient groups were summarised using frequency tables with count and proportion for each category, or mean with the standard deviation (SD) or standard error of the mean (SEM) as appropriate. Differences between groups were tested using Chi-square or Fisher's exact test for nominal endpoints, or the Kruskal-Wallis tests for continuous endpoints. Survival analysis for the three groups STEMI, NSTEMI and UA at 30-day follow-up was performed using the Kaplan Meier-Method for the combined endpoint of MACE. The curves were compared using the logrank-sum test. SPSS software (Chicago, Illinois; Version 20.0) was used for all statistical analysis. A p-value <0.05 was considered as significant. Data are shown as percentages.

Results

Baseline characteristics

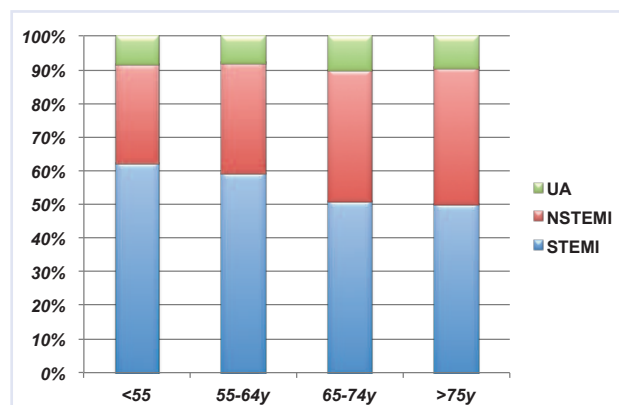
A total of 1,787 patients were included in the Zurich-Acute Coronary Syndromes Registry. Among them, 55.8% (n = 998) had STEMI, 35.3% (n = 631) NSTEMI and 8.8% (n = 158) had UA. The baseline demographic and clinical characteristics are given in table 1.

Patients with STEMI (mean age \pm SD = 62.4 ± 12.5 years) were younger than patients with NSTEMI (65.3 ± 12.2 years) and UA (64.3 ± 12.3 years) ($p < 0.001$) (table 1 and fig. 1), and had fewer cardiovascular risk factors than the patients with NSTEMI and UA. Only smoking was more prevalent in patients with STEMI. A significant difference in cardiovascular risk factors was observed for the three groups of ACS, except for obesity ($p = 0.831$) and a known family history for ACS ($p = 0.053$) (table 1).

Of note, patients with UA were pretreated more aggressively, with preventive medication such as aspirin, beta-blockers and statins, compared to patients with NSTEMI and STEMI. The proportion of patients receiving aspirin was 59.5% (n = 94) in patients with UA, 43.9% (n = 277) in the NSTEMI group and 26.6% (n = 265) in the STEMI group ($p < 0.001$). Similarly, pretreatment with beta-blockers was more common among patients with UA (43.7%; n = 69) when compared with those with NSTEMI (35.2%, n = 222) or STEMI (20.0%, n = 200) ($p < 0.001$). Finally, patients

Figure 1

Frequency of STEMI, NSTEMI and UA stratified by age group. STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST-segment myocardial infarction; UA = unstable angina.



with UA were also more likely to take statins (51.3%; n = 81) than those with NSTEMI (37.4%, n = 236) or STEMI (19.5%, n = 195) ($p < 0.001$). All cardiovascular medications taken prior to admission are summarised in table 1.

After admission, patients with STEMI were more frequently treated with vasopressors (11.0%, n = 110) compared with those with NSTEMI (4.9%, n = 31) or UA (1.3%, n = 2) ($p < 0.001$), and were more often intubated, resuscitated or treated with glycoprotein IIb/

Table 1

Baseline demographic and clinical characteristics of the patients.

	STEMI 998 (55.8%)	NSTEMI 631 (35.3%)	UA 158 (8.8%)	Total 1787	p-value
Male	766 (76.8%)	474 (75.1%)	118 (74.7%)	1358 (76.0%)	0.694
Age (yr; mean \pm SD)	62.4 \pm 12.5	65.3 \pm 12.2	64.3 \pm 12.3	63.6 \pm 12.5	<0.001
Cardiovascular risk factors					
HTN	506 (50.7%)	367 (58.2%)	89 (56.3%)	962 (53.8%)	0.011
DM	145 (14.5%)	139 (22.0%)	32 (20.3%)	316 (17.7%)	<0.001
Hyperlipidaemia	333 (33.4%)	266 (42.2%)	75 (47.5%)	674 (37.7%)	<0.001
Current smoker	465 (46.6%)	230 (36.5%)	59 (37.3%)	754 (42.2%)	<0.001
Obesity	204 (20.4%)	126 (20%)	35 (22.2%)	365 (20.4%)	0.831
FH	242 (24.2%)	152 (24.1%)	52 (32.9%)	446 (25.0%)	0.053
Medication on admission					
Aspirin	265 (26.6%)	277 (43.9%)	94 (59.5%)	636 (35.6%)	<0.001
Clopidogrel	89 (8.9%)	141 (22.3%)	39 (24.7%)	269 (15.1%)	<0.001
Statin	195 (19.5%)	236 (37.4%)	81 (51.3%)	512 (28.7%)	<0.001
Beta-blocker	200 (20.0%)	222 (35.2%)	69 (43.7%)	491 (27.5%)	<0.001
ACE inhibitor	117 (11.7%)	149 (23.6%)	36 (22.8%)	302 (16.9%)	<0.001
Diuretic	120 (12.0%)	159 (25.2%)	44 (27.8%)	323 (18.1%)	<0.001
ARBS	103 (10.3%)	81 (12.8%)	30 (19.0%)	214 (12.0%)	0.005
CCB	79 (7.9%)	65 (10.3%)	18 (11.4%)	162 (9.1%)	0.149
Warfarin	17 (1.7%)	30 (4.8%)	6 (3.8%)	53 (3.0%)	0.002

STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST segment myocardial infarction; UA = unstable angina; HTN = hypertension; DM = diabetes mellitus; FH = known family history; ARBS = angiotensin-receptor blocking agents; CCB = calcium-channel blocker.

Table 2

Acute medication, emergency procedures, haemodynamic parameters and findings at coronary angiography.

	STEMI 998 (55.8%)	NSTEMI 631 (35.3%)	UA 158 (8.8%)	Total 1787	p-value
Acute medication					
Vasopressors	110 (11.0%)	31 (4.9%)	2 (1.3%)	143 (8.0%)	<0.001
GP-IIb/IIIa	295 (29.6%)	89 (14.1%)	13 (8.2%)	397 (22.2%)	<0.001
Emergency procedures					
Intubation	88 (8.8%)	36 (5.7%)	3 (1.9%)	127 (7.1%)	0.002
Resuscitation	117 (11.7%)	34 (5.4%)	5 (3.2%)	156 (8.7%)	<0.001
IABP	126 (12.6%)	51 (8.1%)	4 (2.5%)	181 (10.1%)	<0.001
Unstable	139 (13.9%)	43 (6.8%)	2 (1.3%)	184 (10.3%)	<0.001
Vital signs on admission (mean \pm SD)					
HR (beats per min.)	74.4 \pm 15.6	73 \pm 15.3	68.9 \pm 12.9	73 \pm 15.4	0.001
SBP (mm Hg)	124.4 \pm 27.0	131.1 \pm 27.2	136.6 \pm 26.0	127.7 \pm 27.3	<0.001
DBP (mm Hg)	71.6 \pm 15.3	69.9 \pm 15.2	69.9 \pm 12.8	70.9 \pm 15.1	0.076
Haemodynamic parameters (mean \pmSD)					
LVEDP (mm Hg)	21 \pm 8.8	19.2 \pm 8.0	17.6 \pm 8.0	20 \pm 8.5	<0.001
EF (%)	51.2 \pm 11.6	55.2 \pm 12.0	59.3 \pm 8.7	53.4 \pm 11.8	<0.001
Location of the lesion					
LM	9 (0.9%)	15 (2.4%)	8 (5.1%)	32 (1.8%)	<0.001
LAD	467 (46.8%)	262 (41.5%)	72 (45.6%)	801 (44.8%)	0.112
LCX	126 (12.6%)	177 (28.1%)	47 (29.7%)	350 (19.6%)	<0.001
RCA	383 (38.4%)	151 (23.9%)	25 (15.8%)	559 (31.3%)	<0.001
Graft	13 (1.3%)	26 (4.1%)	6 (3.8%)	45 (2.5%)	0.001
Coronary angiography findings					
Single-vessel disease	512 (51.3%)	238 (37.7%)	69 (43.7%)	819 (45.8%)	<0.001
Multivessel disease	486 (48.7%)	391 (62.0%)	89 (56.3%)	966 (54.1%)	<0.001

STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST segment myocardial infarction; UA= unstable angina; IABP = intra-aortic balloon pump; HR = heart rate; SBP = systolic blood pressure; DP = diastolic blood pressure; LVEDP = left ventricular end-diastolic pressure; EF = ejection fraction; LM = left main artery; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery.

IIIa-inhibitors. In addition, an intra-aortic balloon pump was implanted substantially more often in STEMI patients (12.6%, $n = 126$) than in those with NSTEMI (8.1%, $n = 51$) or UA (2.5%, $n = 4$) ($p < 0.001$). These findings were mirrored by the haemodynamic parameters: patients with STEMI exhibited the lowest systolic blood pressure ($p < 0.001$) and highest heart rate ($p = 0.001$). This was in line with the clinical finding that 13.9% ($n = 139$) of patients with STEMI were in an unstable condition, compared with only 6.8% ($n = 43$) of the NSTEMI and 1.3% ($n = 2$) of the UA patients ($p < 0.001$). Table 2 summarises the acute medication, emergency procedures, haemodynamic parameters and findings at coronary angiography.

Patients with STEMI exhibited the highest plasma total cholesterol levels ($p = 0.017$) and white blood cell counts on admission ($p < 0.001$). C-reactive protein (CRP) on admission was highest in the NSTEMI group, whereas patients with STEMI had the highest peak values. Troponin, creatinine kinase (CK), CK-MB and plasma myoglobin levels were highest in the STEMI group, reflecting more extensive myocardial damage. N-terminales probrain natriuretic peptide (NT-pro-

BNP) values on admission and peak values were higher in the NSTEMI group compared with the STEMI and UA patients ($p < 0.001$). All laboratory values are shown in table 3.

Short-term follow-up

The in-hospital mortality rate was 5.7% ($n = 57$) in the STEMI group, 2.5% ($n = 16$) in the NSTEMI group and lowest at 1.3% ($n = 2$) with UA ($p = 0.001$, fig. 2).

Unplanned revascularisations after discharge were more common in patients with UA (5.7%, $n = 9$) than in those with NSTEMI (2.2%, $n = 14$) or STEMI (2.5%, $n = 25$) ($p = 0.047$). CABG was not different between the three groups (p -value not significant). No difference was found in re-infarction rates between the three groups (STEMI 1.6%, $n = 16$; NSTEMI 0.5%, $n = 3$; UA 1.3%; $n = 2$; $p = 0.120$). Stent thrombosis occurred in 1.1% ($n = 11$) of the STEMI group, and 0.2% ($n = 1$) of the NSTEMI group and 0.6% ($n = 1$) with UA ($p = 0.091$).

Cardiogenic shock was significantly more common in the STEMI group (8.7%, $n = 87$) than with NSTEMI (5.4%, $n = 34$) or UA (0.6%, $n = 1$) ($p < 0.001$). Cardiac

Table 3Laboratory values (mean \pm standard deviation).

	STEMI 998 (55.8%)	NSTEMI 631 (35.3%)	UA 158 (8.8%)	Total 1787	p-value
Cholesterol	4.9 (\pm 0.05)	4.7 (\pm 0.07)	4.6 (\pm 0.14)	4.8 (\pm 0.04)	0.017
HDL	1.1 (\pm 0.02)	1.1 (\pm 0.02)	1.1 (\pm 0.05)	1.1 (\pm 0.01)	0.838
LDL	3.3 (\pm 0.06)	3.0 (\pm 0.07)	2.8 (\pm 0.15)	3.1 (\pm 0.04)	0.002
TG	1.4 (\pm 0.04)	1.5 (\pm 0.06)	1.5 (\pm 0.10)	1.4 (\pm 0.03)	0.014
CRP on admission	15.7 (\pm 1.25)	18.3 (\pm 1.66)	9.5 (\pm 2.04)	16 (\pm 0.93)	<0.001
CRP maximum	60.8 (\pm 3.17)	58.7 (\pm 3.94)	33.1 (\pm 5.27)	57.7 (\pm 2.31)	<0.001
WBC on admission	12.2 (\pm 0.15)	10.0 (\pm 0.16)	8.6 (\pm 0.25)	11.1 (\pm 0.11)	<0.001
WBC maximum	13.7 (\pm 0.17)	11.5 (\pm 0.20)	9.9 (\pm 0.35)	12.6 (\pm 0.13)	<0.001
CK on admission	926.5 (\pm 53.70)	445.6 (\pm 27.68)	167.0 (\pm 24.87)	693.7 (\pm 32.72)	<0.001
CK maximum	2386.5 (\pm 86.96)	870.7 (\pm 51.43)	317.2 (\pm 45.20)	1680.8 (\pm 56.32)	<0.001
CK-MB on admission	114.0 (\pm 5.53)	62.2 (\pm 3.84)	28.0 (\pm 2.88)	88.6 (\pm 3.50)	<0.001
CK-MB maximum	235.7 (\pm 8.57)	100.1 (\pm 5.31)	45.1 (\pm 5.26)	172.1 (\pm 5.53)	<0.001
Myoglobin on admission	745.7 (\pm 44.02)	257.6 (\pm 17.96)	163.6 (\pm 51.30)	532.2 (\pm 27.32)	<0.001
Myoglobin maximum	1284.1 (\pm 71.71)	522.2 (\pm 56.98)	323.2 (\pm 89.04)	945.4 (\pm 47.37)	<0.001
Troponin T on admission	2.0 (\pm 0.16)	0.9 (\pm 0.09)	0.2 (\pm 0.09)	1.5 (\pm 0.10)	<0.001
Troponin T maximum	6.1 (\pm 0.27)	2.2 (\pm 0.15)	4.1 (\pm 3.49)	4.5 (\pm 0.35)	<0.001
NT-proBNP on admission	1758.7 (\pm 183.06)	2535.5 (\pm 253.78)	1895.9 (\pm 571.62)	2027.9 (\pm 144.68)	<0.001
NT-proBNP maximum	3370.5 (\pm 245.68)	3928.3 (\pm 376.26)	2210.7 (\pm 580.05)	3456.9 (\pm 196.65)	<0.001

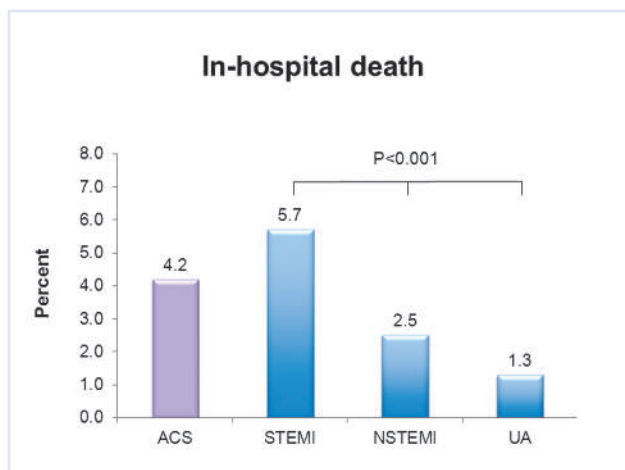
STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST segment myocardial infarction; UA = unstable angina; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TG = triglycerides; CRP = c-reactive protein; WBC = white blood count; CK = creatinine-kinase; BNP = brain-natriuretic peptide.

tamponade was rare and numerically more common in the STEMI group (0.6%, $n = 6$) but was not statistically different from the other groups (0.2% ($n = 1$) with NSTEMI and 0% ($n = 0$) with UA). For septic shock ($p = 0.513$) and stroke ($p = 0.612$), there was no statistically significant difference between the three groups (fig. 3).

Figure 2

In-hospital death rate for the total population of ACS and comparison between STEMI, NSTEMI and UA.

ACS = acute coronary syndrome; STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST-segment myocardial infarction; UA = unstable angina.



At the 30-day follow-up, the rate of MACE was 9.0% ($n = 160$) for the total study population. The prevalence of MACE was higher in the STEMI group (10.6%, $n = 106$) than with NSTEMI (6.7%, $n = 42$) or UA (7.6%, $n = 12$) ($p = 0.020$). Moreover, the Kaplan-Meier survival analysis revealed that the outcomes of STEMI, NSTEMI and UA were indeed substantially different (logrank test $p = 0.018$), in particular for the first days; after approximately 13 days, the survival curves ran in parallel (fig. 4).

Discussion

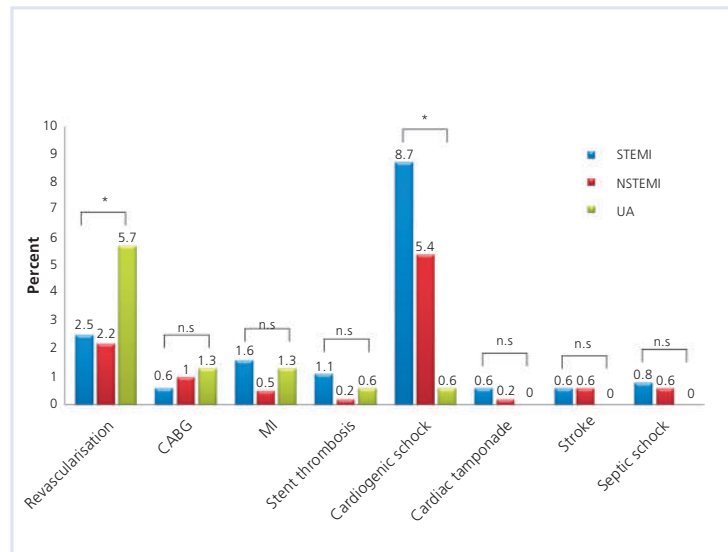
Our results reveal that overall ACS patients enrolled in the Z-ACS registry had a lower 30-day MACE rate and in-hospital mortality compared with the established international GRACE registry [5], which reflects the high quality of the management of this patient population in this tertiary centre.

Our in-hospital mortality rates for STEMI are comparable to the OPERA Registry and Swiss registry of acute coronary syndrome (4.6% and 4.8% for STEMI, respectively) [16, 17], but significantly lower than in the PL-ACS Registry Pilot Group, which revealed an in-hospital mortality rate of 11.6% for STEMI and 8.7% for NSTEMI [18]. We also noted that patients with NSTEMI or UA had a more favourable outcome than patients with STEMI, as frequently reported previ-

Figure 3

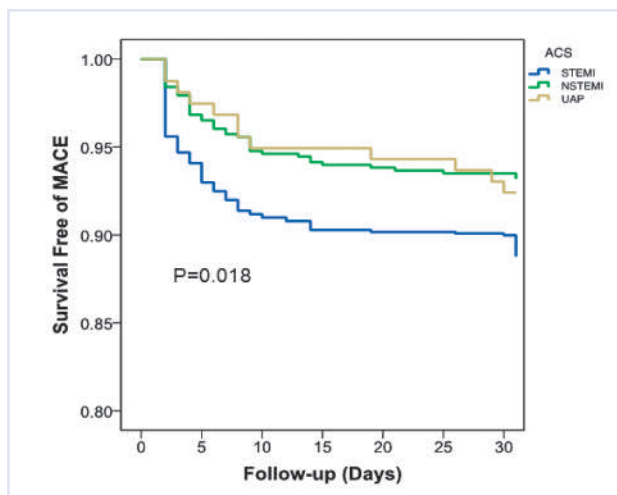
Distribution of complications including, revascularisation, CABG, myocardial infarction, stent thrombosis, cardiac shock, cardiac tamponade, stroke and septic shock between the three groups of ACS.

CABG = coronary artery bypass graft; ACS = acute coronary syndrome.

**Figure 4**

Kaplan Meier survival curves for 30-day MACE rate of the three groups of ACS (STEMI, NSTEMI and UA).

MACE = major adverse cardiac events; ACS = acute coronary syndrome; STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST-segment myocardial infarction; UA = unstable angina.



ously. Indeed, the in-hospital mortality rates were 5.7%, 2.5% and 1.3%, respectively ($p = 0.001$). Also, STEMI patients were more likely to require resuscitation, vasopressors or intubation. This indicates that STEMI patients are a high-risk cohort for whom treatment strategies still make a significant difference to outcome.

It remains still unclear why certain ACS patients present as STEMI and others as NSTEMI or UA. Interestingly, patients with UA, who had the lowest in-hos-

pital mortality, were most commonly pretreated with aspirin, statins and/or beta-blockers on admission. This suggests that when a plaque rupture occurs, patients pretreated with aspirin may develop a smaller clot that is less likely to occlude a major coronary artery, while statin pretreatment may lead to smaller cholesterol cores within the vulnerable lesion resulting in smaller cavities after rupture of a plaque. In line with the latter interpretation, total cholesterol and LDL values were significantly lower in patients with UA, as compared with STEMI and NSTEMI. Of note, optical coherence tomography (OCT) studies have shown that STEMI patients have larger cavities than those with NSTEMI [19]. A previously published study from the GRACE has also demonstrated that preventive cardiovascular premedication can influence the type of ACS presentation [20] and therefore might modulate clinical outcome.

Although difficult to assess in a registry setting, several factors may have contributed to the low complication rates in the Z-ACS registry, including optimal management of ACS patients in a high volume centre with experienced operators. Indeed, volume and operator experience markedly influence ACS outcome [21, 22]. Furthermore, the Zurich metropolitan area is rather small and hospitals are easy to reach. The Zurich area also has a very efficient ambulance system, which further contributes to short-time periods from symptom onset to treatment. Other factors that may have contributed are those that are patient-related, such as age, a major determinant of outcome in ACS [23, 24]. The Z-ACS patients were somewhat younger (mean age for STEMI 62 years, NSTEMI 65 years, UA 64 years) than the GRACE population (STEMI 64 years, NSTEMI 68 years, UA 66 years) [5]. Indeed, in the Z-ACS registry, patients with STEMI were younger, and in the age group below 55 years the rate of STEMI was 28.3%, whereas in the age group over 75 years, only 20.4% presented with STEMI. An increasing frequency of patients with NSTEMI was observed with advanced age, while the frequency of UA was stable over the various age groups. These observations are very similar to the GRACE [5].

Our results are the more impressive because in most trials, and also registries, patients in very poor health with comorbidities and in particular those with cardiogenic shock are usually excluded, which obviously changes reported patient outcomes [25–27]). In the Z-ACS registry, 6.8% of the patients presented in cardiogenic shock, whereas in trials commonly less than 2% of patients exhibited cardiogenic shock. Of note, cardiogenic shock complicates myocardial infarction and accounts for 50%–60% of in-hospital mortality among all age groups [28]. In line with these data, exclusion of patients with cardiogenic shock in the Z-ACS registry would have led to an overall in-hospital mortality of only 1.4%. Similarly, the MACE rate would

have been 4.7% under these conditions. Thus, real-world registries reflect the real world only if all patients with cardiogenic shock or out-of-hospital cardiac arrest are included in the analysis. Furthermore, metropolitan areas with suboptimal ambulance systems may underestimate their true mortality in ACS as many patients may not reach the hospital in time. Be that as it may, our results again demonstrate that there is still room for improvement in the management of patients with cardiogenic shock, who represent a highest risk subset. These patients would benefit most from new treatment strategies.

It is important to note that our patient cohort only included patients from one tertiary care centre with a high quality medical service. However, the GRACE registry contains a total of 18 cluster sites in 14 countries including newly industrialised countries. Undoubtedly, healthcare disparities affect the infrastructure and lead to inferior outcomes, in this case pertaining to cardiovascular disease. Switzerland has one of the best healthcare systems in the world, which translates into high-quality care, as demonstrated by the Deloitte Centre for Health Solutions 2010 survey "Health care consumers in Switzerland 2010". For instance, with the advent of drug-eluting stents (DES), studies have shown that patients with STEMI undergoing primary angioplasty have better long-term outcomes for up to 4 years as compared with those receiving bare-metal stents. In this regard, it is of interest that in Switzerland, DES were utilised in 91% of all patients in 2007 [29]. A recent randomised trial of Swiss centres comparing biolimus-eluting and bare metal stents in patients with STEMI indeed showed that DES are associated with better outcome [27]. At our institution, the use of DES based quality report was between 2007 and 2010 above 80%.

Furthermore, appropriate medical pretreatment may affect outcome. Indeed, a report published by Stauffer et al., using data from the Acute Myocardial Infarction Swiss-Plus (AMIS Plus) registry, found, as in a similar Austrian study [30], that patients pretreated with combination of clopidogrel and percutaneous coronary intervention (PCI) had significantly lower morbidity and mortality, which may not be the case in settings with limited access to resources [31].

One limitation of our single-centre study was the retrospective and observational nature. However, the allcomer design potentially minimised selection bias. In this regard, many prospective, randomised, controlled trials do not enrol all consecutive patients owing to exclusion criteria or missing informed consent. Here we present a reliable, allcomer registry in which all in-hospital events were carefully reported. However, data on long-term follow-up are lacking and only limited information on medical assessments such as door-to-balloon time, percentage of TIMI flow and rate of multivessel PCIs was available.

In summary, registries can serve as effective tools for evaluating outcomes and clinical practice. They are able to demonstrate to what degree the highest standards of evidence-based care are used and what impact they have on outcome. Our results provide such an insight and strongly suggest that outcome must particularly be improved in patients with cardiogenic shock, who contribute the most to morbidity and mortality in ACS. Furthermore, they strongly suggest that preventive medication with aspirin, statins and beta-blockers may protect from STEMI, the clinical presentation with the worst outcome.

Acknowledgment: The authors are grateful to Raphael B. Haller, Robin Halioua and Armin Handzic for data collection.

References

- 1 Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD. Third Universal Definition of Myocardial Infarction. *Journal of the American College of Cardiology* 2012.
- 2 Libby P. Current concepts of the pathogenesis of the acute coronary syndromes. *Circulation*. 2001;104:365–72.
- 3 Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD. Third universal definition of myocardial infarction. *Nat Rev Cardiol*. 2012.
- 4 Smith SC, Jr., Collins A, Ferrari R, et al. Our Time: A Call to Save Preventable Death From Cardiovascular Disease (Heart Disease and Stroke). *Circulation*. 2012.
- 5 Steg PG, Goldberg RJ, Gore JM, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients hospitalized with acute coronary syndromes in the Global Registry of Acute Coronary Events (GRACE). *Am J Cardiol*. 2002;90:358–63.
- 6 Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). *Eur Heart J*. 2012.
- 7 Fox KA, Goodman SG, Klein W, et al. Management of acute coronary syndromes. Variations in practice and outcome; findings from the Global Registry of Acute Coronary Events (GRACE). *Eur Heart J*. 2002;23:1177–89.
- 8 Caro JJ, Migliaccio-Walle K. Generalizing the results of clinical trials to actual practice: the example of clopidogrel therapy for the prevention of vascular events. CAPRA (CAPRIE Actual Practice Rates Analysis) Study Group. Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events. *Am J Med*. 1999;107:568–72.
- 9 Steg PG, Lopez-Sendon J, de Sa EL, et al. External validity of clinical trials in acute myocardial infarction. *Arch Intern Med*. 2007;167:68–73.
- 10 Bosch X, Delgado V, Verbal F, et al. Causes of ineligibility in randomized controlled trials and long-term mortality in patients with non-ST-segment elevation acute coronary syndromes. *Int J Cardiol*. 2008;124:86–91.
- 11 Rationale and design of the GRACE (Global Registry of Acute Coronary Events) Project: a multinational registry of patients hospitalized with acute coronary syndromes. *Am Heart J*. 2001;141:190–9.
- 12 Eagle KA, Goodman SG, Avezum A, Budaj A, Sullivan CM, Lopez-Sendon J. Practice variation and missed opportunities for reperfusion in ST-segment-elevation myocardial infarction: findings from the Global Registry of Acute Coronary Events (GRACE). *Lancet*. 2002;359:373–7.
- 13 Urban P, Radovanovic D, Erne P, et al. Impact of changing definitions for myocardial infarction: a report from the AMIS registry. *Am J Med*. 2008;121:1065–71.
- 14 Jeger RV, Radovanovic D, Hunziker PR, et al. Ten-year trends in the incidence and treatment of cardiogenic shock. *Ann Intern Med*. 2008;149:618–26.
- 15 Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. *Circulation*. 2012;126:2020–35.
- 16 Montalescot G, Dallongeville J, Van Belle E, et al. STEMI and NSTEMI: are they so different? 1 year outcomes in acute myocardial infarction as defined by the ESC/ACC definition (the OPERA registry). *Eur Heart J*. 2007;28:1409–17.

- 17 Radovanovic D, Erne P. AMIS Plus: Swiss registry of acute coronary syndrome. *Heart*. 2010;96:917–21.
- 18 Polonski L, Gasior M, Gierlotka M, et al. A comparison of ST elevation versus non-ST elevation myocardial infarction outcomes in a large registry database: are non-ST myocardial infarctions associated with worse long-term prognoses? *Int J Cardiol*. 2011;152:70–7.
- 19 Ino Y, Kubo T, Tanaka A, et al. Difference of culprit lesion morphologies between ST-segment elevation myocardial infarction and non-ST-segment elevation acute coronary syndrome: an optical coherence tomography study. *JACC Cardiovasc Interv*. 2011;4:76–82.
- 20 Spencer FA, Santopinto JJ, Gore JM, et al. Impact of aspirin on presentation and hospital outcomes in patients with acute coronary syndromes (The Global Registry of Acute Coronary Events [GRACE]). *Am J Cardiol*. 2002;90:1056–61.
- 21 Kastrati A, Neumann FJ, Schomig A. Operator volume and outcome of patients undergoing coronary stent placement. *J Am Coll Cardiol*. 1998;32:970–6.
- 22 Vakili BA, Kaplan R, Brown DL. Volume-outcome relation for physicians and hospitals performing angioplasty for acute myocardial infarction in New York state. *Circulation*. 2001;104:2171–6.
- 23 Granger CB, Goldberg RJ, Dabbous O, et al. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med*. 2003;163:2345–53.
- 24 Gharacholou SM, Lopes RD, Alexander KP, et al. Age and outcomes in ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: findings from the APEX-AMI trial. *Arch Intern Med*. 2011;171:559–67.
- 25 Gross CP, Mallory R, Heiat A, Krumholz HM. Reporting the recruitment process in clinical trials: who are these patients and how did they get there? *Ann Intern Med*. 2002;137:10–6.
- 26 King SB, 3rd, Barnhart HX, Kosinski AS, et al. Angioplasty or surgery for multivessel coronary artery disease: comparison of eligible registry and randomized patients in the EAST trial and influence of treatment selection on outcomes. Emory Angioplasty versus Surgery Trial Investigators. *Am J Cardiol*. 1997;79:1453–9.
- 27 Raber L, Kelbaek H, Ostojic M, et al. Effect of biolimus-eluting stents with biodegradable polymer vs bare-metal stents on cardiovascular events among patients with acute myocardial infarction: the COMFORTABLE AMI randomized trial. *JAMA*. 2012;308:777–87.
- 28 Hochman JS. Cardiogenic shock complicating acute myocardial infarction: expanding the paradigm. *Circulation*. 2003;107:2998–3002.
- 29 Maeder MT, Windecker S, Roffi M, Kaiser CA, Stauffer JC, Pedrazzini G, et al. Interventional Cardiology in Switzerland during the year 2007. *Cardiovascular Medicine*. 2010;13:18–24.
- 30 Dorler J, Edlinger M, Alber HF, et al. Clopidogrel pre-treatment is associated with reduced in-hospital mortality in primary percutaneous coronary intervention for acute ST-elevation myocardial infarction. *Eur Heart J*. 2011;32:2954–61.
- 31 Stauffer JC, Goy JJ, Duvoisin N, Radovanovic D, Rickli H, Erne P. Dramatic effect of early clopidogrel administration in reducing mortality and MACE rates in ACS patients. Data from the Swiss registry AMIS-Plus. *Swiss Med Wkly*. 2012;142:w13573.